

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 45-47, 49-59, 61-82 and 85-91 are pending in the application, with claims 45, 46, 58, 59, 72, 85 and 91 being the independent claims. Claims 48, 83 and 84 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 85-91 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Support for Amended and New Claims

Support for amended claims 45 and 46 can be found throughout the specification, for example, at page 2, line 16 through page 3, line 14. Support for amended claims 58 and 59 can be found throughout the specification, for example, at page 9, line 15 through page 10, line 4, and at page 11, lines 15-16. Support for amended claim 62 can be found throughout the specification, for example, at page 13, lines 20-27. Support for amended claim 70 can be found throughout the specification, for example, at page 10, lines 6-9. Support for amended claim 72 can be found throughout the specification, for example, at page 9, line 15 through page 10, line 14, and in original claim 31. Support for new claims 85-87 can be found throughout the specification, for example, at page 11, lines 15-16, at page 13, lines 20-

26, and in original claims 36-38. Support for new claims 88-90 can be found throughout the specification, for example, at page 14, lines 1-4. Support for new claim 91 can be found throughout the specification, for example, at page 2, line 16 through page 3, line 14, at page 16, line 23 through page 17, line 4, and at page 51, line 6 through page 54, line 14.

II. Oath/Declaration

The Examiner has acknowledged Applicants' desire to hold the matter of the Oath/Declaration in abeyance. *See* Paper No. 31, page 2. The Examiner stated, however, that the present Oath/Declaration remains defective for the reasons made of record in the Office Action mailed on April 12, 1999 (paper No. 2). *See* Paper No. 31, page 2. Applicants maintain their request that the matter of the Oath/Declaration be held in abeyance until the remaining issues outstanding in this application are resolved.

III. Obviousness-Type Double Patenting

Claims 45-59, 61-71 and 81-84 were rejected under the judicially created doctrine of obviousness-type double patenting. *See* Paper No. 31, page 3. Applicants again respectfully request that this rejection be held in abeyance until the remaining outstanding issues in this application are resolved.

IV. Claim Rejection Under 35 U.S.C. § 103

Claims 72, 76 and 77 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bogoslovakaia *et al.*, *Epidemiol. Immunobiol.* 12:65-68 (1984) (hereinafter "Bogoslovakaia"), in view of Sambrook *et al.*, "Molecular Cloning: A Laboratory Manual,"

Sambrook *et al.* eds., Cold Spring Harbor Laboratory Press, 1989, pp. 1.74-1.84 (hereinafter "Sambrook"), Binger *et al.*, U.S. Patent No. 5,661,015 (hereinafter "Binger") and Ron, U.S. Patent No. 4,404,186 (hereinafter "Ron"). *See* Paper No. 31, page 4. Applicants respectfully traverse this rejection.

The Examiner asserted that Bogoslovakaia teaches *E. coli* possessing a membrane having an increased unsaturated fatty acid content relative to total fatty acid content. *See* Paper No. 31, pages 4-5. It was acknowledged that Bogoslovakaia does not teach competent *E. coli*, *see id.* at page 6.

The Examiner also cited Sambrook, Binger and Ron. *See* Paper No. 31, page 6. Sambrook was cited as teaching a method for making competent *E. coli*. Binger was cited as teaching the use of certain transformed *E. coli* as a live vaccine for vaccination of poultry. Ron was cited as teaching the use of *E. coli* for live vaccines and for teaching that live vaccines can be administered as aerosols. According to the Examiner:

At the time the invention was filed, it would have been obvious to one of ordinary skill in the art to make competent either strain of Bogoslovakaia *et al* having an increased % of unsaturated fatty acid in the membrane. One of ordinary skill in the art would have been motivated to do so in order to prepare a live vaccine comprising a vector expressing an antigen for a costly disease in poultry and using a bacteria which has an increased survivability in air would be advantageous because it would improve the efficacy of aerosol administration by increasing the number of surviving microbes per aerosol dose.

Paper No. 31, page 6. Applicants respectfully submit that the Examiner's rationale for the rejection under 35 U.S.C. § 103 is legally insufficient.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the references or to combine reference teachings. *See In re Rouffet*,

149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). The evidence demonstrating a motivation to combine references must be "clear and particular." *See In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). "Broad conclusory statements regarding the teaching of multiple references, standing alone, are not 'evidence.'" *Id.*, 175 F.3d at 999, 50 USPQ2d at 1617. Moreover, "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988). Here, there is no suggestion or motivation to combine the references cited by the Examiner. Thus, the rejection under § 103 was improper and should be withdrawn.

At the outset, Applicants note that the rejection is based on the Examiner's assertion that "the property of enhanced transformation ability will be inherent to the bacteria" of Bogoslovakaia. *See* Paper No. 31, pages 5-6. The asserted "inherent" properties of a reference, however, cannot be relied upon to support a rejection under § 103. *See In re Spormann*, 150 USPQ 449, 452 (CCPA 1966). That which is inherent cannot be obvious, since inherent information "is not necessarily known . . . [and] Obviousness cannot be predicated on what is unknown." *Id.* Thus, the asserted "inherent" properties of the bacteria of Bogoslovakaia cannot be relied upon to support the rejection under § 103.

The Examiner stated that the use of bacteria having increased survivability in air "would be advantageous because it would improve the efficacy of aerosol administration by increasing the number of surviving microbes per aerosol dose." Paper No. 31, page 6. The references cited by the examiner, however, do not indicate or suggest a need for increasing the number of surviving microbes per aerosol dose in bacterial vaccines. For instance, there is nothing in Ron indicating a reduction in bacterial viability in the aerosol vaccine described

therein. In fact, Ron states that "[i]mmunization by application of an aerosol of the vaccine is a very convenient and *effective* route of immunization by this type of vaccine." *See* Ron at column 5, lines 19-21 (emphasis added).

Binger does not suggest modifying the *E. coli* described therein in view of any of the other cited references. There is nothing in Binger that would specifically suggest combining the disclosure with that of either Ron, Bogoslovakaia or Sambrook.

Finally, the Examiner has not explained why a person of ordinary skill in the art would have been motivated to combine or modify Sambrook in view of Bogoslovakaia. In fact, the Examiner has not explained how Sambrook might possibly relate to any of the other cited references at all. Thus, it is unclear how Sambrook was intended to contribute to a finding of obviousness.

In summary, the rejection is improper because it is based on the asserted inherent properties of the bacteria of Bogoslovakaia, and obviousness cannot be predicated upon a teaching alleged to be inherent in a reference. *See Spormann*, 150 USPQ at 452. In addition, the Examiner has not presented any specific evidence to indicate or suggest that a person of ordinary skill in the art would have been motivated to modify the disclosure of Bogoslovakaia or to combine it with that of any other cited reference. Therefore, a *prima facie* case of obviousness cannot be established with respect to any of the currently pending claims, including the newly added claims. *See Rouffet*, 149 F.3d at 1357, 47 USPQ2d at 1457-58. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

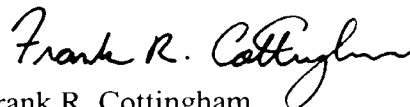
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

45. (Four times amended) A method for enhancing the transformation ability [and] or the viability of a bacterium, said method comprising:

- (a) increasing the unsaturated fatty acid content of the membrane of said bacterium by
 - (i) enhancing expression of one or more genes that encode one or more gene products which increase said unsaturated fatty acid content, or
 - (ii) genetically selecting for a bacterium having an increased membrane unsaturated fatty acid content, and
- (b) storing said bacterium at a temperature of from about +4°C to about -80°C,

wherein said bacterium, after said storing, exhibits enhanced transformation ability [and] or enhanced viability relative to the transformation ability [and] or viability exhibited by said bacterium prior to increasing its unsaturated fatty acid content.

46. (Four times amended) A method for enhancing the transformation ability [and] or the viability of bacteria, said method comprising:

- (a) increasing the unsaturated fatty acid content of the membrane of said bacteria by

- (i) enhancing expression of one or more genes that encode one or more gene products which increase said unsaturated fatty acid content, or
 - (ii) genetically selecting for a bacterium having an increased membrane unsaturated fatty acid content, and
- (b) storing said bacteria at a temperature of from about +4°C to about -80°C,

wherein said bacteria, after said storing, exhibit enhanced transformation ability [and] or enhanced viability relative to the transformation ability [and] or viability exhibited by said bacteria prior to increasing their unsaturated fatty acid content.

49. (Once amended) The method of claim [48] 46, wherein said enhancing expression comprises increasing transcription or translation of said one or more genes.

50. (Twice amended) The method of claim [48] 46, wherein said enhancing expression comprises increasing the copy number of one or more genes, wherein said one or more genes are comprised by one or more vectors.

56. (Once amended) The method of claim [48] 46, wherein said one or more genes are selected from the group consisting of a *fabB* gene, a *fabF* gene, a *fabD* gene, a *fabG* gene, a *fabA* gene, a *fabI* gene, a *fabZ* gene, a *fadA* gene, a *fadB* gene, a *fadE* gene, a *fadL* gene, a *fadR* gene, a *farR* gene, and a *fatA* gene.

58. (Thrice amended) A method for obtaining [enhancing the transformation ability of] a competent bacterium, said method comprising:

- (a) increasing the unsaturated fatty acid content of the membrane of [said] a bacterium by
 - (i) enhancing expression of one or more genes that encode one or more gene products which increase said unsaturated fatty acid content, or
 - (ii) genetically selecting for a bacterium having an increased membrane unsaturated fatty acid content; and
- (b) making said bacterium competent [storing said bacterium at a temperature of from about +4°C to about -20°C,

wherein said bacterium, after said storing, exhibits enhanced transformation ability relative to the transformation ability exhibited by said bacterium prior to increasing its unsaturated fatty acid content].

59. (Thrice amended) A method for obtaining [enhancing the transformation ability of] competent bacteria, said method comprising:

- (a) increasing the unsaturated fatty acid content of the membrane of [said] bacteria by
 - (i) enhancing expression of one or more genes that encode one or more gene products which increase said unsaturated fatty acid content, or

(ii) genetically selecting for bacteria having an increased membrane unsaturated fatty acid content; and

(b) making said bacteria competent [storing said bacteria at a temperature of from about +4°C to about -20°C,

wherein said bacteria, after said storing, exhibit enhanced transformation ability relative to the transformation ability exhibited by said bacteria prior to increasing their unsaturated fatty acid content].

62. (Thrice amended) The method of claim 59, wherein said enhancing expression comprises increasing the copy number of said one or more genes[, wherein said one or more genes are comprised by one or more vectors].

70. (Twice amended) The method of claim 47, wherein said bacteria exhibit enhanced transformation ability [and] or enhanced viability after storage at about -20°C.

72. (Twice amended) A competent *E. coli* possessing a membrane having an increased unsaturated fatty acid content relative to total fatty acid content, wherein said competent *E. coli* exhibits enhanced transformation ability [after storage at a temperature of from about +4°C to about -20°C] relative to the transformation ability exhibited by said competent *E. coli* prior to increasing its unsaturated fatty acid content.

Claims 48, 83 and 84 are sought to be cancelled.

Claims 85-91 are sought to be added.